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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte LOUIS D. FALO JR., and KENNETH L. ROCK

Appeal No. 2001-0507
Application No. 08/931,219

ON BRIEF

Before SCHEINER, ADAMS, and MILLS, Administrative Patent Judges.

ADAMS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on the appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 1-3, 5-17, 19-32, 34-47, 49-61, and 63-71, which are all the claims pending in the application.

Claims 1, 68 and 71 are illustrative of the subject matter on appeal and is reproduced below:

1. An in vivo method of treating a mammalian host capable of generating an immune response, which comprises:

(a) generating a DNA fragment which expresses an antigenic protein or antigenic protein fragment;

(b) distributing said DNA fragment on a particle surface, resulting in a particulate polynucleotide;

(c) inoculating said mammalian host with said particulate polynucleotide; and

(d) delivering said particulate polynucleotide to the cytoplasm of an antigen presenting cell within said mammalian host, such that said expressed antigenic protein or antigenic protein fragment is presented to the membrane surface of said antigen presenting cell through the MHC class I pathway, wherein said presentation of said antigenic protein or protein fragment elicits an anti-tumor or anti-viral immune response in said host that destroys neoplastic or virally infected cells.

68. A method for transfecting an antigen presenting cell comprising:

(a) distributing a DNA fragment which expresses an antigenic protein or fragment thereof on a particle surface, resulting in a particulate polynucleotide;

(b) delivering said particulate polynucleotide to the cytoplasm of an antigen presenting cell, such that said expressed antigenic protein or fragment thereof is presented to the membrane surface of said antigen presenting cell.

71. A method of inducing a CTL immune response in a mammalian host capable of generating an immune response, comprising the step of transfecting antigen presenting cells of said host in vivo with a DNA fragment which expresses an antigenic protein or fragment thereof, such that said antigenic protein or fragment thereof is presented to the membrane surface of said antigen presenting cell through the MHC class I pathway and tumor cells are destroyed.

The references relied upon by the examiner are[1]:

Weiner et al. (Weiner) 5,593,972 Jan. 14, 1997

Tang et al. (Tang), "Genetic Immunization is a Simple Method for Eliciting an Immune Response," Nature, Vol. 356, No. 6365, pp. 152-54 (1992)

Barry et al. (Barry '94), "Production of Monoclonal Antibodies by Genetic Immunization," Bio Techniques, Vol. 16, No. 4, pp. 616-18 (1994)

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[1] According to the examiner (Answer, page 4), Paul was "[c]ited to set forth immunological facts in response to appellant's [sic] assertions in art rejections[]." In addition, the examiner cites Condon (Answer, page 16) to emphasize that "[i]t is well known that the skin tissue (epidermis) is prevalent with dendritic cells (antigen presenting cells)...." As such we do not consider the introduction of these references as evidence of the prior well known statement made by the examiner as constituting a new ground of rejection. Furthermore, appellants had an opportunity to address references in their Reply Brief. In addition, appellants waived any objection that the Answer contained an impermissible new ground of rejection by not timely petitioning the issue. See MPEP 1208.01.

Hui et al. (Hui), "Generation of Allo-Reactive Cytotoxic T Lymphocytes by Particle Bombardment-Mediated Gene Transfer," J. Immunol. Methods, Vol. 171, No. 2, pp. 147-55 (1994)

Condon et al. (Condon), " DNA-based immunization by in vivo transfection of Dendritic Cells," Nature Medicine, Vol. 2, pp. 1122 (1996)

Barry et al. (Barry '97), "Biological Features of Genetic Immunization," Vaccine, Vol. 15, No. 8, pp. 788-91 (1997)

(Paul), Fundamental Immunology, pp. 121 and 593 (William E. Paul ed., Raven Press, New York, 3rd Ed. 1993)

GROUNDS OF REJECTION

Claims 1-3, 5-17, 19-32, 34-47, 49-61 and 63-71 stand rejected under 35 U.S.C. § 112, first paragraph, as being based on an insufficient disclosure to support or enable the full scope of the claimed invention.

Claims 1, 15, 29, 68, 69 and 71 stand rejected under 35 U.S.C. 102(b) as anticipated by Tang, or Barry '94.

Claims 1, 15, 29, and 68-71 stand rejected under 35 U.S.C. 102(b) as anticipated by Hui.

Claims 1-3, 5-17, 19-32, 34-47, 49-61 and 63-71 stand rejected under 35 U.S.C. § 103 as being unpatentable over Weiner in view of either Tang or Barry '94.

We reverse the rejection under 35 U.S.C. § 112, first paragraph, the rejection of claims 1, 15, 29 and 71 under 35 U.S.C. § 102(b) as anticipated by Tang, Barry '94 or Hui; and the rejection of claims 29-32, 34-47, 49-61 and 63-67 under 35 U.S.C. § 103 as being unpatentable over Weiner in view of either Tang or Barry '94.

We affirm the rejection of claims 68 and 69 under 35 U.S.C. § 102(b) as anticipated by Tang, or Barry '94; the rejection of claims 68-70 under 35 U.S.C. § 102(b) as anticipated by Hui; and the rejection of claims 1-3, 5-14, 15-17, 19-28, and 68-71 under 35 U.S.C. § 103 as being unpatentable over Weiner in view of either Tang or Barry '94.

DISCUSSION

THE REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH:

According to the examiner (Answer, page 7), "the claimed methods are only enabled for gene gun[] delivery (biolistic approach) into skin or direct injection into the subcutaneum, and are not enabled for any other routes of administration, particularly since dendritic cells are most prevalent in skin tissue." The examiner finds (Answer, page 6), "the specification fails to teach or provide sufficient guidance for routes of administration other than into skin or the subcutaneum." The examiner reasons (id.) that while "skin tissue (epidermis) is prevalent with dendritic cells", "intramuscular and intravascular routes of administration have not been shown by the art or by the specification to be sufficient for targeting antigen presenting cells." According to the examiner (Answer, page 7), Barry '97 "compare efficiency of genetic vaccination by intramuscular ... injection vs. gene gun into the epidermis (skin) and conclude that gene gun is more effective for eliciting an immune response per unit DNA." Based on this evidence, the examiner concludes (id.) that Barry '97 "fail[s] to support that i.m. injection (or any other route of administration) of particulate polynucleotides (as recited in the claims) would result in delivery to antigen

presenting cells such that presentation causes an MHC class I immune response...."

In response appellants argue (Reply Brief, bridging paragraph, pages 2-3):

> Barry ['97] does not appear to discuss inoculation with particulate polynucleotides at all, either by i.m. injection or a biolistic device; in fact, Barry ['97] appears to be inoculating with a DNA plasmid both by gene gun and i.m. injection. Appellants respectfully submit that it is therefore disingenuous to state that Barry ['97] fails to support i.m. injection of particulate polynucleotides, when Barry ['97] does not appear to discuss injection of particulate polynucleotides by any manner; his silence cannot be extrapolated to mean a lack of support.

In addition, appellants argue (Reply Brief, page 3), "[t]he [e]xaminer ignores the statements made by Barry ['97] supporting the use of i.m. injection. For example, Barry ['97] also states that 'both routes of immunization can be routinely used with μg amounts of plasmid ...' and that while the gene gun may be more efficient, 'i.m. injection has its own advantages.'"

Accordingly, appellants conclude (id.), "the Barry ['97] article does not provide the requisite evidence that [a]ppellants' specification lacks enablement." We agree. Similarly, we are not persuaded by the examiner's reliance on Condon. To satisfy the enablement requirement of 35 U.S.C. § 112, first paragraph, a patent application must adequately disclose the claimed invention so as to enable a person skilled in the art to practice the invention at the time the application was filed without undue experimentation. Enzo Biochem, Inc. v. Calgene, Inc., 188 F.3d 1362, 1371-72, 52 USPQ2d 1129, 1136 (Fed. Cir. 1999). We note, however, that "nothing more than objective enablement is

required, and therefore it is irrelevant whether this teaching is provided through broad terminology or illustrative examples." In re Marzocchi, 439 F.2d 220, 223, 169 USPQ 367, 369 (CCPA 1971). As set forth in In re Wright, 999 F.2d 1557, 1561-62, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993):

> When rejecting a claim under the enablement requirement of section 112, the PTO bears an initial burden of setting forth a reasonable explanation as to why it believes that the scope of protection provided by that claim is not adequately enabled by the description of the invention provided in the specification of the application; this includes, of course, providing sufficient reasons for doubting any assertions in the specification as to the scope of enablement.

On this record we find no Wands[2]-type analysis by the examiner. Furthermore, as discussed supra, the evidence relied upon by the examiner fails to demonstrate that the claimed invention is non-enabled throughout its entire scope. In this regard, we remind the examiner that nothing more than objective enablement is required, and therefore it is irrelevant whether this teaching is provided through broad terminology or illustrative examples. Marzocchi, 439 F.2d at 223, 169 USPQ at 369.

Therefore, it is our opinion that the examiner failed sustained her burden of establishing a prima facie case of non-enablement. The burden of proof does not shift to appellant until the examiner first meets her burden. Marzocchi,

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[2] In re Wands, 858 F.2d 731, 735, 736-37, 8 USPQ2d 1400, 1402, 1404 (Fed. Cir. 1988), the factors to be considered in determining whether a claimed invention is enabled throughout its scope without undue experimentation include the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claims.

439 F.2d at 223-224, 169 USPQ at 369-370. Accordingly, we reverse the rejection of claims 1-3, 5-17, 19-32, 34-47, 49-61 and 63-71 under 35 U.S.C. § 112, first paragraph, as being based on an insufficient disclosure to support or enable the full scope of the claimed invention.

THE REJECTIONS UNDER 35 U.S.C. § 102:

As set forth in Gechter v. Davidson, 116 F.3d 1454, 1457, 43 USPQ2d 1030, 1032 (Fed. Cir. 1997), "[u]nder 35 U.S.C. § 102, every limitation of a claim must identically appear in a single prior art reference for it to anticipate the claim."

Tang or Barry '94:

As we understand appellants' claim groupings (Brief, page 3), claims 68 and 69 stand or fall together. Accordingly, we limit our discussion to representative independent claim 68. Claim 69 will stand or fall together with claim 68. In re Young, 927 F.2d 588, 590, 18 USPQ2d 1089, 1091 (Fed. Cir. 1991). In addition, appellants' claim groupings require (id.) that claims 1, 15, 29, 68 and 71 stand or fall separately.

Claims 1, 15, 29 and 71:

The examiner finds (Answer, page 8), Tang teach the direct injection of microparticles coated with DNA encoding human growth hormone and with DNA encoding α-1 antitrypsin into skin results in the production of antibodies.[3]

[3] Similarly, the examiner finds (Answer, page 9), Barry '94 teach the direct injection of a microprojectiles coated with DNA encoding human growth hormone into skin results in the production of antibodies.

Therefore, the examiner concludes (Answer, page 9), Tang's methods "meet all of the limitations of the claims in that each and every step recited in the claims is taught by Tang ... and any effect by following each step taught by Tang et al. is an inherent effect."[4] Apparently the examiner is relying on the general rule that merely discovering and claiming a new benefit of an old process cannot render the process again patentable. In re Swinehart, 439 F.2d 210, 213, 169 USPQ 226, 229 (CCPA 1971).

The examiner, however, recognizes that Tang do not teach a method wherein an anti-tumor or anti-viral immune response is elicited in the host that destroys neoplastic or virally infected cells. In this regard, "it is the [e]xaminer's position that any effect of the method steps is inherent, however, Tang et al. do discuss how the generation of antibodies by genetic immunization in animals could guard against pathogenic infection by producing foreign antigens in restricted subsets of self-cells that mimic natural infections." Answer, bridging paragraph, pages 8-9.[5]

However, with regard to both Tang and Barry '94 the examiner fails to identify how antibodies to human growth hormone and α-1 antitrypsin are inherently a response that destroys neoplastic or virally infected cells. We remind the examiner that an anticipating reference "must disclose every element of the challenged claim and enable one skilled in the art to make the anticipating

[4] The examiner makes the same finding with regard to Barry '94. See Answer, bridging paragraph, pages 9-10.
[5] The examiner does not make a similar finding in Barry '94, she just maintains that it is her position that any effect of the method steps is inherent. See Answer, page 9.

subject matter." PPG Industries, Inc. v. Guardian Industries Corp., 75 F.3d 1558, 1566, 37 USPQ2d 1618, 1624 (Fed. Cir. 1996). When anticipation is based on inherency of limitations not expressly disclosed in the assertedly anticipating reference, it must be shown that the undisclosed information was known to be present in the subject matter of the reference. Continental Can Co. USA, Inc. v. Monsanto Co., 948 F.2d 1264, 1269, 20 USPQ2d 1746, 1749-50 (Fed. Cir. 1991). We recognize the examiner's attempt to side step her burden of demonstrating that the effect achieved by Tang's method is inherently the same as appellants, wherein the examiner emphasizes Tang's suggestion that genetic immunization could guard against pathogenic infection. We are, however, not persuaded. Instead we remind the examiner that an inherent limitation is one that is necessarily present; invalidation based on inherency is not established by "probabilities or possibilities." Scaltech, Inc. v. Retec/Tetra, LLC., 178 F.3d 1378, 1384, 51 USPQ2d 1055, 1059 (Fed. Cir. 1999). Therefore, the fact that Tang suggests that genetic immunization might guard against pathogenic infection is not sufficient to establish inherency and thus is not sufficient to anticipate claims 1, 15, 29 and 71. While, as the examiner recognizes (Answer, page 22), "the claims are not limited to any specific antigen..." the claims do require the antigen elicit an anti-tumor or anti-viral immune response in said host that destroys neoplastic or virally infected cells. The examiner has not demonstrated that this requirement of the claimed invention is met by either Tang or Barry '94.

We also note, as do appellants (Brief, page 7), that the examiner has incorrectly interpreted the claim limitation of "direct injection," as set forth in claim

29, "as encompassing both direct injection using a gene-gun as well as direct injection without use of a gene-gun." Answer, page 9 and 10. We wish to emphasize that not only do appellants' claims distinguish between "direct injection" see e.g., claim 29 and inoculating using a biolistic device see e.g., claim 15, but appellants' specification distinguishes between the two terms. See specification, page 15, "[a] mammalian host may be immunized ... by a biolistic ... delivery procedure.... In another embodiment of the present invention a mammalian host is immunized ... by direct injection, including but not limited to subcutaneous injection, epidermal injection, dermal injection, lymphatic injection and intra venous injection." Accordingly, the examiner has incorrectly construed appellants' claimed invention.

For the foregoing reasons we reverse the rejection of claims 1, 15, 29 and 71 under 35 U.S.C. 102(b) as anticipated by Tang, or Barry '94.

Claim 68:

Claim 68, however, stands on different footing. Claim 68 is drawn to a method of transfecting an antigen presenting cell (APC). Unlike, claims 1, 15, 29, and 71, there is no requirement in claim 68 that the transformed APC stimulate an immune response capable of eliciting an anti-tumor or anti-viral immune response in said host that destroys neoplastic or virally infected cells.

As set forth in Barry '94 (page 616, column 2) microprojectiles were coated with CMV-hGH. CMV-hGH was created by inserting the genomic sequence of hGH into the BamHI site of pcDNA I. Id. Similarly, Tang teach (page 152, column 2, footnotes omitted), "microprojectiles coated with plasmids

containing the genomic copy of the human growth hormone ... gene under the transcriptional control of either the human β-actin promoter or the cytomegalovirus ... promoter." Therefore, both Barry '94 and Tang teach step (a) of the claimed method -- "distributing a DNA fragment which expresses an antigenic protein or fragment thereof on a particle surface, resulting in a particulate polynucleotide."

Page 15 of appellants' specification discloses that "[a] mammalian host may be immunized with a particulate polynucleotide by a biolistic ... delivery procedure such that the particulate polynucleotide specifically enters host cells, including APCs...." As emphasized by the examiner both Tang (Answer, page 8) and Barry '94 (Answer, page 9) teach the use of biolistic delivery. Therefore, both Barry '94 and Tang teach step (b) of the claimed method – "delivering said particulate polynucleotide to the cytoplasm of an antigen presenting cell, such that said expressed antigenic protein or fragment thereof is presented to the membrane surface of said antigen presenting cell."

In response, appellants argue (Brief, page 7) that the references do not teach delivery of an antigenic protein or fragment thereof to APCs. However, as discussed supra, in addition to pages 9 and 10 of the Answer, Tang and Barry '94 teach each and every step of the claimed method and any effect achieved by following each step taught by either reference is an inherent effect. Stated differently, the foregoing discussion demonstrates that the natural result flowing from the teachings of either Tang or Barry '94 would be the delivery of particulate polynucleotide to the cytoplasm of an antigen presenting cell, such that said

expressed antigenic protein or fragment thereof is presented to the membrane surface of said antigen presenting cell. See In re Oelrich, 666 F.2d 578, 581-82, 212 USPQ 323, 326 (CCPA 1981), quoting Hansgirg v. Kemmer, 102 F.2d 212, 214, 40 USPQ 665, 667 (1939) (if the disclosure is sufficient to show that the natural result flowing from the operation as taught would result in the performance of the questioned function, it seems to be well settled that the disclosure should be regarded as sufficient to demonstrate inherency.).

We also note appellants' argument (Reply Brief, page 3) that the methods of Tang and Barry '94 require the presence of "[a]n external source of antigenic protein ... to elicit an antibody response; this external source is not required according to the present methods." While this external source of antigenic protein "is not required" by appellants', claimed methods, it is also not excluded by the transitional phrase "comprising." Consequently, we are not persuaded by this argument.

Therefore, it is our opinion that the examiner met her burden of establishing a prima facie case of anticipation based on inherency. After the PTO establishes a prima facie case of anticipation based on inherency, the burden shifts to appellants to "prove that the subject matter shown to be in the prior art does not possess the characteristic relied on." In re Swinehart, 439 F.2d 210, 212-13, 169 USPQ 226, 229 (CCPA 1971). Accord In re Fitzgerald, 619 F.2d 67, 70, 205 USPQ 594, 596 (CCPA 1980), quoted with approval in In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985); In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433-34 (CCPA 1977);

In re Ludtke, 441 F.2d 660, 664, 169 USPQ 563, 566 (1971). On this record, appellants failed to meet their burden.

Accordingly we affirm the rejection of claim 68 under 35 U.S.C. 102(b) as anticipated by Tang, or Barry '94. As discussed supra claim 69 falls together with claim 68.

Hui:

As we understand appellants' claim groupings (Brief, page 3), claims 68-70 stand or fall together. Accordingly, we limit our discussion to representative independent claim 68. Claims 69 and 70 will stand or fall together with claim 68. Young. In addition, appellants' claim groupings require (id.) that claims 1, 15, 29, 68 and 71 stand or fall separately.

Claims 1, 15, 29, and 71:

While the examiner emphasizes (Answer, bridging sentence, pages 10-11) that Hui "report that the immunized spleen cells gave a 3-4 fold increase in the anti-H-2kb CTL response compared to non-immunized control mice," the examiner fails to recognize that this 3-4 fold increase in response occurred only after restimulation in vitro. Hui, page 154, column 2, citing Table 4. Accordingly, Hui do not anticipate claims 1, 15, or 71, which require induction of an immune response in a mammalian host.

In addition, we note that the examiner finds (Answer, page 10), Hui teach direct injection of DNA encoding H-2k^b into a mouse spleen, in situ, by use of a gene-gun (a biolistic approach). At page 11 of the Answer, the examiner states "the term 'direct injection' is interpreted as encompassing both direct injection

using a gene-gun as well as direct injection without use of a gene-gun." However, as discussed, supra, appellants have distinguished between "direct injection" and inoculation by use of a "biolistic device" or "gene-gun". Therefore, claim 29 which requires inoculation "direct injection" is not anticipated by Hui.

Accordingly we reverse the rejection of claims 1, 15, 29, and 71 under 35 U.S.C. § 102(b) as anticipated by Hui.

Claim 68:

Again, claim 68 stands on different footing. Claim 68 is drawn to a method of transfecting an antigen presenting cell (APC). Unlike, claims 1, 15, 29, and 71, there is no requirement in claim 68 that a response be obtained in a mammalian host.

As set forth in Hui (page 148, column 2) plasmid DNA was precipitated onto tungsten particles. The plasmid DNA was obtained by cloning H-2K^b full-length cDNA into the pcDNA1 plasmid which contains a CMV promoter and enhancer, splice segment and polyadenylation signal, an SV40 and a Polyoma virus eukaryotic origin of replication. Id. at column 1. Therefore, Hui teach step (a) of the claimed method -- "distributing a DNA fragment which expresses an antigenic protein or fragment thereof on a particle surface, resulting in a particulate polynucleotide."

Page 15 of appellants' specification discloses "[a] mammalian host may be immunized with a particulate polynucleotide by a biolistic ... delivery procedure such that the particulate polynucleotide specifically enters host cells, including APCs...." As emphasized by the examiner (Answer, page 10) Hui

teach the use of biolistic delivery. In addition, Hui confirm (page 152, column 1), by FACS analysis that cells isolated from inoculated spleens expressed H-2K^b molecules, with the highest level of expression occurring 6-8 days after inoculation. We note the examiner's reference to Paul (Answer, page 24) to confirm that the spleen contains a sufficient amount of antigen processing cells to present protein antigen effectively. We also note, the appellants do not contest this reference in their Reply Brief, but instead refer to their arguments on Brief (see Reply Brief, page 4). Therefore, in our opinion the evidence of record weighs in favor of the examiner's position. Therefore, Hui teach step (b) of the claimed method – "delivering said particulate polynucleotide to the cytoplasm of an antigen presenting cell, such that said expressed antigenic protein or fragment thereof is presented to the membrane surface of said antigen presenting cell."

In response, appellants argue (Brief, page 7) that the references do not teach delivery of an antigenic protein or fragment thereof to APCs. However, as discussed supra, in addition to page 11 of the Answer, Hui teach each and every step of the claimed method and any effect achieved by following each step taught by either reference is an inherent effect. Stated differently, the foregoing discussion demonstrates that the natural result flowing from the teachings of Hui would be the delivery of particulate polynucleotide to the cytoplasm of an antigen presenting cell, such that said expressed antigenic protein or fragment thereof is presented to the membrane surface of said antigen presenting cell. See Oelrich.

That anti-H-2K^b activity was seen only after restimulation in vitro (Brief, page 8) is of no consequence with regard to claim 68, which contains no limitation excluding or requiring such activity. Nor is their any requirement in claim 68 that the method result in antitumor or antiviral immunity. See id.

Therefore, it is our opinion that the examiner met her burden of establishing a prima facie case of anticipation based on inherency. Thus the burden was properly shifted to appellants. On this record, appellants failed to meet their burden.

Accordingly we reverse the rejection of claim 68 under 35 U.S.C. § 102(b) as anticipated by Hui. As set forth supra, claims 69 and 70 fall together with claim 68.

THE REJECTION UNDER 35 U.S.C. § 103:

According to appellants (Brief, page 3):

> Claims 1-3 and [5]-14 stand or fall together; [c]laims 15-17 and 19-28 stand or fall together ...; [c]laims 29-32 and 34-43 stand or fall together ...; [c]laims 44-47 and 49-58 stand or fall together ...; [c]laims 59-61 and 63-67 stand or fall together ...; [c]laims 68-70 stand or fall together ...; and [c]laim 71 stands or falls alone.

Accordingly, we limit our discussion to representative independent claims 1, 15, 29, 44, 59, 68 and 71. Claims 2, 3 and 5-14 will stand or fall together with claim 1; claims 16, 17 and 19-28 will stand or fall together with claim 15; claims 30-32 and 34-43 stand or fall together with claim 29; claims 45-47 and 49-58 stand or fall together with claim 44; claims 60, 61 and 63-67 stand or fall together with claim 59; and claims 69 and 70 will stand or fall together with claim 68. Young.

According to the examiner (Answer, page 12), Weiner teach methods of genetic immunization against tumors, viral and bacterial pathogens, including HIV gp160 and the human neu oncogene. In addition, the examiner finds (id.), Weiner disclose that their genetic immunization protocol is more likely to elicit a CTL response then other methods of immunization known in the art and that the immune response resulting from their methodology is capable, by virtue of CTL's, of completely eliminating tumors. According to the examiner (Answer, page 13), Weiner differs from the claims in that "they do not specifically teach the use of particulate polynucleotides", or "the biolistic approach" to genetic immunization. Nevertheless, the examiner finds (id.), Weiner suggest and discuss the application of the biolistic approach of genetic immunization and that "an increase in efficiency of the immune response ... may be achieved by use of a direct DNA delivery system such as particle bombardment."

The examiner relies (id.) on Tang and Barry '94 to demonstrate that "it was routine knowledge in the genetic immunization art to deliver DNA encoding target antigens of interest by means of particle bombardment."

Claims 29, 44, and 59:

We recognize the examiner's rationale for combining Tang or Barry '94 with Weiner (Answer, page 14), specifically:

> it would have been [prima facie] obvious for one of ordinary skill in the art, at the time the claimed invention was made to modify the genetic immunization protocol of Weiner et al. by applying particle bombardment rather than direct injection. One of ordinary skill in the art would have been sufficiently motivated to make such a modification, particularly since Weiner et al. suggest the result of the use of particle bombardment would be an increase in the

> efficiency of the immune response generated by genetic immunization.

We also recognize, the examiner's finding (Answer, page 13) that Weiner does not teach particulate polynucleotides.

With note that claims 29, 44, and 59 require that a mammalian host be inoculated with particulate polynucleotide by direct injection. Since the examiner found that Weiner does not teach the direct injection of particulate polynucleotides and that a one would be motivated to use "particle bombardment rather than direct injection" we cannot agree with the examiner that it would have been obvious to combine Weiner with either Tang or Barry '94 to obtain the method of claims 29, 44 and 59.

Accordingly we reverse the rejection of claims 29, 44 and 59 under 35 U.S.C. § 103 as being unpatentable over Weiner in view of either Tang or Barry '94. As set forth supra, claims 30-32 and 34-43 stand with claim 29; claims 45-47 and 49-58 stand with claim 44; and claims 60, 61 and 63-67 stand with claim 59.

Claims 1, 15, 68 and 71:

In deciding patentability issues under 35 U.S. C. § 103, the court observed in Panduit Corp. v. Dennison Manufacturing Co., 810 F.2d 1561, 1567-68, 1 USPQ2d 1593, 1597 (Fed. Cir.), cert. denied, 481 U.S. 1052 (1987), "[a]nalysis begins with a key legal question--what is the invention claimed?" since "[c]laim interpretation ... will normally control the remainder of the decisional process." In this regard, we note that the only difference between claim 1 and

claim 15 is that claim 15 is expressly limited to inoculation by use of a biolistic device, while claim 1 is generic to the method of inoculating – "inoculating said mammalian host with said particulate polynucleotide" – and therefore claim 1 reads on the use of a biolistic device. Claims 68 and 71 are also generic to the method by which the antigen presenting cell is transfected.

We note that Weiner disclose (column 1, lines 15-18), their "invention relates to the introduction of DNA molecules into an individual's tissues or cells that then can produce proteins capable of eliciting an immune response." Stated differently, Weiner's invention is directed to an in vivo method of treating a mammalian host capable of generating an immune response, as is appellants' claimed method. According to Weiner (Column 6, lines 31-41, and Column 8, lines 17-50), genetic material that encodes an immunogenic peptide or protein[6] is operatively linked to regulatory sequences and directly administered to an individual in vivo. The genetic material is then expressed by the individual's cells to form immunogenic target proteins that elicit an immune response. The target antigens produced within the cells of the host are processed intracellularly: broken down into small peptides, bound by Class I MHC molecules, and expressed on the cell surface. Thus, genetic immunization according to Weiner's invention is capable of eliciting cytotoxic T-cell (CTL) responses. Column 8, lines 45-47.

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[6] According to Weiner (Column 8, lines 24-26) the genetic material encodes a peptide or protein that shares at least an epitope with an immunogenic protein to be targeted. According to the examiner (Answer, page 12), Weiner teach (e.g., examples 1-47 and tables 1 & 2) a number of target antigens including HIV gp160 and the human neu oncogene.

Weiner's genetic constructs can be administered in a variety of ways including microprojectile bombardment gene guns – "a biolistic device." As the examiner points out (Answer, pages 13-14), both Tang and Barry '94 teach that it was routine knowledge in the genetic immunization art that particulate polynucleotide is used to inoculate a mammalian host using a biolistic device. In this regard, we recognize that Weiner incorporate U.S. Patent No. 4,945,050 by reference to teach a microprojectile particle bombardment procedure. Column 20, lines 32-36. In addition, Weiner also disclose that particle bombardment may increase the efficiency of their method. See Column 32, lines 54-56.

Based on the foregoing evidence, it is our opinion that the examiner has set forth the evidence necessary to demonstrate that the prior art, when viewed as a whole, suggested the desirability, and thus the obviousness of making the prior art combination.

In response, appellants argue (Brief, bridging sentence, pages 8-9), "Weiner does not teach the use of DNA vaccines or particulate polynucleotides for use in particle bombardment." As discussed supra, Weiner discloses the use of microprojectile bombardment gene guns as a means to administer the genetic constructs. Column 17, lines 5-18. Therefore, notwithstanding appellants' argument (Brief, page 9) that Weiner's statement with regard to increased efficiency is a "speculative sentence," Weiner included particle bombardment as an intended means of administering his genetic constructs. Also discussed supra, Tang and Barry '94 demonstrate that it was routine knowledge in the

genetic immunization art that particulate polynucleotide is used to inoculate a mammalian host using a biolistic device. Accordingly, we are not persuaded by appellants' argument.

Despite appellants' argument (Brief, page 9) that "Tang and Barry '94 utilize particle bombardment to elicit an antibody response, not a response through the MHC Class I pathway as recited by [a]ppellants" and therefore does not overcome the alleged shortcomings of Weiner, Tang and Barry '94 which look only at antibody response and do not address the mechanism by which an immune response is generated. As discussed supra, Weiner clearly disclose the mechanism by which an immune response is generated. According to Weiner (Column 6, lines 31-41, and Column 8, lines 17-50), genetic material that encodes an immunogenic peptide or protein is operatively linked to regulatory sequences and directly administered to an individual in vivo. The genetic material is then expressed by the individual's cells to form immunogenic target proteins that elicit an immune response. The target antigens produced within the cells of the host are processed intracellularly: broken down into small peptides, bound by Class I MHC molecules, and expressed on the cell surface. Thus, genetic immunization according to Weiner's invention is capable of eliciting cytotoxic T-cell (CTL) responses. Column 8, lines 45-47. Therefore, contrary to appellants' argument (Brief, page 9), one skilled in the art would conclude that such methods would result in the elicitation of a response through the MHC Class I pathway, because Weiner expressly states that is will.

We also note appellants' argument (Reply Brief, page 4) that "[w]hile [a]ppellants' claims may not preclude the use of ... [bupivacaine], that [a]ppellants' methods achieve their desired elicitation of a CTL response without the use of such an agent represents an advance not taught by the art." Notwithstanding appellants' position, the claims remain open and, as appellants' recognize, do not preclude the use of such an agent. Stated differently, appellants' arguments are not commensurate in scope to the claimed invention.

As a whole, we are not persuaded by appellants' arguments, instead it remains our opinion that the examiner has set forth the evidence necessary to demonstrate that the prior art, when viewed as a whole, suggested the desirability, and thus the obviousness of making the prior art combination. Accordingly we affirm the rejection of claims 1, 15, 68 and 71 under 35 U.S.C. § 103 as being unpatentable over Weiner in view of either Tang or Barry '94. As set forth supra, claims 2, 3, 5-17, 19-28, 69, 70 and 71 fall together with claims 1, 15, 68 and 71.

SUMMARY

The following rejections are affirmed:

- The rejection of claims 68 and 69 under 35 U.S.C. § 102(b) as anticipated by Tang, or Barry '94.
- The rejection of claims 68-70 under 35 U.S.C. § 102(b) as anticipated by Hui.
- The rejection of claims 1-3, 5-14, 15-17, 19-28, and 68-71 under 35 U.S.C. § 103 as being unpatentable over Weiner in view of either Tang or Barry '94.

We reverse all other rejections of record.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED-IN-PART

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